Supreme Court, U.S.
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No. 06-1249

IN THE
Supreme Court of the United States

WYETH,

Petitioner,

v.

DIANA LEVINE,

Respondent.

On Petition for a Writ of Certiorari to the Supreme Court of Vermont

RESPONDENT'S BRIEF IN OPPOSITION

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QUESTION PRESENTED

The Vermont Supreme Court below affirmed an award of compensatory damages to respondent Diana Levine. As the case comes to this Court, petitioner Wyeth does not challenge that, as a matter of Vermont law, Ms. Levine's arm was amputated because Wyeth failed to warn against using a method of administering its anti-nausea drug Phenergan that causes precisely the type of injury that Ms. Levine sustained.

The question presented is

Should this Court grant review to consider whether the Food and Drug Administration's approval of the labeling for Phenergan impliedly preempts the award of compensatory damages to Ms. Levine where

(a) no appellate court has ever adopted the position advanced by Wyeth;

(b) the Vermont Supreme Court found, as a matter of fact, that the FDA never considered, let alone rejected, a warning to preclude use of the method of administration that caused Ms. Levine's injuries;

(c) an FDA regulation permits a drug manufacturer, without FDA approval, to revise an existing label to "add or strengthen an instruction about dosage or administration that is intended to increase the safe use of the drug"; and

(d) the 2006 FDA regulatory preamble on which Wyeth relies for its claim of preemption does not, by its terms, apply to the circumstances of this case, and was not issued until *after* the FDA approved the label at issue here?

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INTRODUCTION

On April 7, 2000, respondent Diana Levine, a professional musician, went to the hospital for treatment of a headache and, after being injected with a drug manufactured by petitioner Wyeth, left with injuries that led quickly and irreversibly to the loss of her right arm. Specifically, Ms. Levine's arm had to be amputated because Wyeth's drug Phenergan, prescribed to alleviate nausea associated with a migraine headache, reached Ms. Levine's arteries. Wyeth knew that arterial contact causes the exact injuries Ms. Levine sustained. Phenergan was given to Ms. Levine using a method of administration that was consistent with, and not precluded by, Wyeth's label instructions and that Wyeth knew risked contact with Ms. Levine's arteries. Because Wyeth did not warn against that method of administration in its drug labeling or otherwise, a Vermont jury awarded Ms. Levine compensatory damages, and the Vermont Supreme Court affirmed.

The question presented by Wyeth – whether the Food and Drug Administration's approval of a prescription drug label preempts state-law damages actions premised on "differing labeling judgments" – is not worthy of review for a fundamental reason embodied in this Court's Rule 10: Although the FDA's drug approval process and the states' traditional common-law civil justice systems have co-existed for nearly 70 years, not a single federal or state appellate court has ever held that a state-law failure-to-warn verdict is preempted by the federal laws governing the marketing and labeling of prescription drugs. To the contrary, every appellate court to have addressed the question has held that a state-law damages claim based on a drug manufacturer's failure to warn is not preempted by federal law.

Moreover, even if the Court were inclined to consider the question presented by Wyeth, *this case* does not present it. Wyeth's petition is premised on the factual assertion that the

FDA specifically considered and rejected a warning on the method of administration for Phenergan that Ms. Levine claimed would have prevented her injuries. The purported differences between the FDA's commands with respect to Phenergan's label and the duty-to-warn that Ms. Levine claimed entitled her to damages created, in Wyeth's view, an impermissible conflict between federal and state law. But Wyeth's factual claim is simply not accurate. The Vermont Supreme Court held, *as a matter of fact*, that Wyeth's assertions regarding FDA's label decisions were unsupported by "any evidence," Pet. App. 16a, and that the record contained no basis for Wyeth's claim that the FDA had considered, let alone rejected, the warning that Ms. Levine claimed would have prevented her injuries. *See id.* at 17a-19a. The Vermont Supreme Court's understanding of the factual record is correct, and, in any event, this Court should not grant review to consider a legal issue that would only be reached if the Court were first to overturn a state court's factual determinations.

This case is an inappropriate vehicle for considering the question presented for another reason as well. Wyeth rests its preemption argument in large part on the purported preemptive power of an FDA regulatory preamble issued in 2006. Pet. 11-12, 15, 27-30. Even assuming that Wyeth were correct that the FDA's preamble supports its position regarding preemption and that the preamble filled a statutory gap or clarified a statutory ambiguity entitling it to judicial deference – both positions with which we disagree – any federal legal command created by the preamble could not have had legal effect until 2006, years after the approval of the Phenergan label.

Finally, there is good reason why no appellate court has ever embraced Wyeth's position. The Food, Drug, and Cosmetic Act (FDCA) bars preemption unless there is a "direct and positive conflict" between federal and state law. Pub. L.

87-781, § 202, 76 Stat. 780, 793 (1962). Moreover, FDA regulations provide that FDA-approved drug "labeling *shall* be revised to include a warning as soon as there is reasonable evidence of an association of a serious hazard with a drug," 21 C.F.R. § 201.80(e) (emphasis added), and affirmatively permit manufacturers, without prior FDA approval, to amend labels to "add or strengthen an instruction about dosage and administration that is intended to increase the safe use of the drug product." 21 C.F.R. § 314.70(c)(6)(iii)(C). Thus, the circumstances under which FDA regulation could conflict with a state-law damages action are very narrow, if not non-existent. Review should be denied for that reason as well, particularly in the absence of a division among the appellate courts.

STATEMENT OF THE CASE

A. Factual Background

On April 7, 2000, Diana Levine received injections of Wyeth's prescription drug Phenergan to treat nausea associated with a migraine headache. The drug was first administered by intramuscular injection. Pet. App. 2a. Later that day, the drug was administered intravenously through a technique known as direct IV, or "IV push." *Id.* In this method, a syringe pushes medication directly into the patient's vein. The method is called "direct" to distinguish it from a more common means of intravenous administration in which the medication is placed into a stream of saline flowing from a hanging IV bag. Tr. vol. I, at 194. Wyeth has known for decades that when Phenergan is administered by the IV push method, even by experienced clinicians, inadvertent arterial contact can result. *Id.* at 218-24; *see also id.* at 216 (referring to at least 20 reported cases "where Phenergan has caused an amputation," all resulting from IV push). Based on undisputed expert testimony, the trial court found as fact that

> [o]ne way to reduce the risk of inadvertent intra-arterial injection is to set up a free-flowing IV bag and introduce the drug into the IV solution. This is an alternative to injection through the [IV push] infusion set into a patient's vein. Administration through a free-flowing IV bag reduces the risk of inadvertent arterial injection because the nurse or physician can be more certain that the needle has been placed in a vein. A solution dripping from an IV bag will not flow freely into an artery due to back pressure from the patient.

Pet. App. 52a-53a (fact #4, citing Tr. vol. I, at 194-98, 208-14); *see also, e.g.*, Tr. vol. I, at 195-97 (Dr. Harold Green) (explaining that use of hanging IV involves virtually no risk of arterial exposure and is "far safer" than IV push).

Wyeth has also known that when Phenergan comes in contact with an artery, the artery dies, and necrosis, gangrene, and amputation result. Four experts testified that if Phenergan is used intravenously, it should be done only through a hanging IV bag and that the label should have precluded use of IV push. *Id.* vol. I, at 230-33; vol. II, at 28, 73-74, 97-98, 111. One of Wyeth's experts acknowledged that he would hesitate to use direct IV injection for use in non-life-threatening situations and, at his deposition, stated that he would have written the label to instruct that Phenergan be administered into a running, established IV. *Id.* vol. IV, at 168-69. Another Wyeth expert agreed with Ms. Levine's expert that it was safer to administer Phenergan through a free-flowing IV than through the direct method. *See* Pet. App. 55a (fact #13). On Phenergan's label, however, use of the IV push method is not foreclosed, contraindicated, or even mentioned. And, as the Vermont Supreme Court held, the FDA never considered any warning

regarding the safety (or lack thereof) of the IV push method. *Id.* at 16a-19a.[1]

Because the IV push method was used to administer Phenergan to Ms. Levine, the drug penetrated her artery. Pet. App. 2a. For seven weeks after the injection, Ms. Levine suffered unimaginable physical and emotional pain as she watched her right hand turn black and die. *Id.*; Tr. vol. III, at 38 (Dr. Mark Bucksbaum) ("Pain scales usually are run from one to ten. This is a ten. ... there's not much worse than this type of scenario."), at 165-66 (Ms. Levine describing excruciating pain, terror, and fear of dying and losing her arm). In short, as a result of being subjected to an unsafe and unnecessary method of administration of a drug to curb nausea, Ms. Levine endured two amputations. She first lost her right hand and then her right arm up to the elbow, which forever destroyed her ability to play music – her profession and lifelong passion.

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[1]Without citing any authority, let alone any FDA findings, the petition (at 8 & n.3) lauds the efficacy of IV push for its alleged speed of administration and ability to combat nausea and dehydration, suggesting that the FDA sanctioned the IV push method for these reasons. No record evidence supports that suggestion. The evidence at trial demonstrated that although IV administration may provide somewhat faster relief from nausea, that small benefit does not warrant the risk of *IV push* administration. *See, e.g.*, Tr. vol. I, at 184 (Dr. John Mathew) ("the enormous risk – even though the odds might be small in any one instance – is nowhere near offset by the small gain of 15 to 20 minutes less vomiting or nausea."); vol. II, at 81-82 (Jessica Fisch, P.A.) ("It can work faster, but that's not an excuse for taking somebody's arm and having some kind of extravasation injury that means they lose their fingers or their arm. It's nausea. It's not – this isn't – a heart attack, this is somebody who's sick to their stomach."). The notion that an *IV push* administration of *Phenergan* was necessary to prevent dehydration is also at odds with the record. The evidence showed that vomiting emergency room patients are hydrated by administering a dripping IV containing a solution that may or may not include a drug to counteract the vomiting. *See* Tr. vol. I, at 197-98 (Dr. Harold Green).

B. The FDA Drug Approval Process, The FDCA's Relationship With State Law, And Approval Of The Phenergan Label.

1. FDA Approval And Drug Labeling

Since enactment of the FDCA in 1938, new prescription drugs must be approved by the FDA before they are marketed. From 1938 to 1962, new drugs were approved after an FDA review regarding the drug's safety. Since 1962, drugs are reviewed for efficacy as well, which, as Wyeth put it below, "enabl[ed] FDA to balance risks against benefits." Br. for Defendant-Appellant, at 11, in *Levine v. Wyeth*, No. 2004-384 (Vt. S. Ct. filed Jan. 19, 2004). As the Vermont Supreme Court explained, a manufacturer seeking to market a prescription drug must file a new drug application (NDA) with the FDA. Pet. App. 9a (citing 21 U.S.C. § 355(a)). The agency must approve the NDA "unless it fails to meet certain criteria, including whether test results and other information establish that the drug is 'safe for use under the conditions prescribed, recommended, or suggested in the proposed labeling thereof,' whether there is 'substantial evidence that the drug will have the effect it purports or is represented to have under the conditions of use prescribed, recommended, or suggested in the proposed labeling thereof,' and whether, 'based on a fair evaluation of all material facts, such labeling is false or misleading in any particular.'" *Id.* (quoting 21 U.S.C. § 355(d)).

Because prescription drug labeling provides information used by clinicians to prescribe and administer an approved drug, the FDA's regulations describe in detail the proper form and content for labeling. *See generally* 21 C.F.R. Part 201. Once a drug is approved by the agency, it generally must be accompanied by labeling in the form approved by the FDA. *See* 21 C.F.R. § 314.70(b)(2)(v). The label's content is not, however, set in stone. Rather, a manufacturer is *required* to

alter its labeling in certain circumstances. FDA regulations provide that approved drug "labeling *shall* be revised to include a warning as soon as there is reasonable evidence of an association of a serious hazard with a drug[.]" *Id.* § 201.80(e) (emphasis added). Moreover, the FDA is not required to approve all label changes before drug manufacturers make them. Manufacturers are permitted to revise labels, without prior FDA approval, to

> add or strengthen a contraindication, warning, precaution, or adverse reaction; [and to] add or strengthen an instruction about dosage and administration that is intended to increase the safe use of the drug product[.]

Id. § 314.70(c)(6)(iii)(A), (C); *see also* 44 Fed. Reg. 37434, 37447 (1979) (noting that revised warnings may be made by various means, including via label changes and "Dear Doctor" letters).

2. The Relationship Between Federal Drug Regulation And State Law

Throughout the nearly 70 years since enactment of the FDCA, the states' traditional common-law tort systems have compensated injured persons for injuries caused by prescription drugs. As enacted in 1938, the FDCA was silent regarding its effect on state law and did not suggest that state-law damages claims of any kind would be preempted; indeed, "Congress rejected a provision in a draft of the original FD&C Act providing a federal cause of action for damages [for injuries caused by prescription drugs] because 'a common law right of action [already] exists.'" Robert Adler & Richard Mann, *Preemption and Medical Devices: The Courts Run Amok*, 59 Mo. L. Rev. 895, 924 & n.130 (1995). Thereafter, when enacting the 1962 FDCA requirements regarding drug efficacy,

Congress included the following provision regarding preemption:

> Nothing in the amendments made by this Act to the federal Food, Drug, and Cosmetic Act shall be construed as invalidating any provision of State law which would be valid in the absence of such amendments unless there is a direct and positive conflict between such amendments and such provision of State law.

Pub. L. No. 87-781, § 202.

Until recently, the FDA had never suggested that state-law products liability suits constituted such "a direct and positive conflict." To the contrary, on at least two occasions, the FDA took the opposite view. In 1979 and 1998, in preambles accompanying drug regulations, the agency stated that state tort law did not interfere with federal regulation. *See* 63 Fed. Reg. 66378, 66384 (1998) (regulation addressing Medication Guides, issued pursuant to FDA's authority over drug labeling) ("FDA does not believe that the evolution of state tort law will cause the development of standards that would be at odds with the agency's regulations."); 44 Fed. Reg. at 37437 ("It is not the intent of the FDA to influence the civil tort liability of the manufacturer.").

In December 2000, the FDA proposed a new regulation to address the form and content of drug labeling, the principal purpose of which was to require a new "Highlights" section on drug labels. At that time, the agency noted that "this proposed rule does not preempt State law." 65 Fed. Reg. 81082, 81103 (2000). In 2006, in finalizing these labeling rules, the agency took a different view, claiming in the regulatory preamble that, in narrow circumstances, the FDA's approval of a drug's labeling may preempt a state tort claim based on a failure to warn. The agency stated that

> FDA believes that State laws conflict with and stand as an obstacle to achievement of the full objectives and purposes of Federal law when they purport to compel a firm to include in labeling or advertising a statement that FDA has considered and found scientifically unsubstantiated . . . [or when State law] purports to preclude a firm from including in labeling or advertising a statement that is included in prescription drug labeling.

71 Fed. Reg. 3922, 3935 (2006), Pet. App. 136a.

3. History Of The Phenergan Label

The drug approval process necessarily involves some back-and-forth between the drug manufacturer and the FDA, as the manufacturer submits proposed labeling with its NDA and the FDA must respond. Phenergan and its labeling were first approved by the FDA in 1955, before the agency had authority over drug efficacy. Although the petition paints a history of intense interaction between Wyeth and the FDA regarding the labeling for Phenergan, it was nothing of the sort. In the more than 50 years since Phenergan's approval, the record reveals only two related sets of interactions between the FDA and Wyeth regarding the Phenergan label. Both were apparently triggered by Wyeth's 1981 submission of a supplemental NDA in response to an agency-wide effort to revise drug labeling. *See* Pet. 7. The first interaction culminated in 1987 with a revised warning concerning the already-known and undisputed adverse effects of inadvertent arterial exposure to Phenergan. Pet. App. 150a-157a. This interaction between Wyeth and the FDA did not concern the method of administration of Phenergan in general, or the IV push method in particular. *See id.*

Second, as part of the FDA's review, Wyeth was required to submit proposed labeling for Phenergan, which

necessarily included all of the topics reflected in the original label, including warnings about inadvertent arterial exposure. As part of that submission, Wyeth proposed wording for the instruction concerning administration of Phenergan through a hanging IV bag that was somewhat different from the label in current use. Neither version concerned the IV push method. *See* Pet. App. 4a-5a n.1 (comparing current label with proposal). In a 1997 letter, issued some 16 years after Wyeth's original submission, the FDA, without any explanation, directed Wyeth to "retain [the] verbiage in [the] current label" with regard to inadvertent arterial exposure. Pet. App. 162a. *Id.*

In sum, none of the exchanges between Wyeth and the FDA even mentions the IV push method of administration, and Wyeth presented no evidence at trial that it or the FDA ever considered amending the Phenergan label to address the safety or efficacy of the IV push method.

C. The Proceedings Below

Ms. Levine brought suit against Wyeth in Vermont Superior Court to recover compensation for her life-altering injuries. As noted earlier, at trial, medical experts testified that Wyeth should have precluded use of the IV push method because of its potentially devastating consequences. The jury found Wyeth liable for failing to warn clinicians not to use that method and awarded compensation to Ms. Levine for her economic and non-economic losses. The trial court denied Wyeth's motion for judgment in its favor on federal preemption grounds, both at the close of evidence and post-verdict. Pet. App. 49a.

The Vermont Supreme Court affirmed, holding that Ms. Levine's claims are not preempted by the federal law. The court began by noting Wyeth's acknowledgment that the FDCA does not expressly preempt state law nor occupy the field of prescription drug regulation, and thus focused its analysis on

Wyeth's contention that Ms. Levine's recovery was impliedly preempted because it "actually conflicts with federal law." Pet. App. 8a (quoting *Cipollone v. Liggett Group, Inc.*, 505 U.S. 504, 516 (1992)).[2]

The Vermont Supreme Court then explained that in light of 21 C.F.R. § 314.70(c)(6)(iii) – the regulation that permits manufacturers to add or strengthen a contraindication or warning, or add or strengthen an instruction about dosage and administration, without FDA approval – there is no general "conflict between federal labeling requirements and state failure-to-warn claims." Pet. App. 11a. As the court put it: "Section 314.70(c) allows, and arguably encourages, manufacturers to add and strengthen warnings that, despite FDA approval, are insufficient to protect consumers. State tort claims simply give these manufacturers a concrete incentive to take this action as quickly as possible." *Id.*

The court then rejected Wyeth's assertion that the FDA's actions with respect to the Phenergan label preempted Ms. Levine's claims on the ground that Wyeth's position lacked any support in the factual record. The court found no evidence that the FDA considered the safety (or lack thereof) of the IV push method of administration. *See generally id.* at 16a-19a; *see also, e.g., id.* at 17a ("Neither the letters [exchanged

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[2]At oral argument, Wyeth's counsel emphasized that its claim of conflict preemption was quite narrow and turned solely on what Wyeth maintained were facts peculiar to this case:

> I want to emphasize to the Court that the issue as presented here is very narrow and very particularized. . . . It's focused on Phenergan in the facts of this case. Wyeth is not contending for field preemption, for the ouster of Vermont law, tort law [is] not at issue here . . . nor are we arguing that the mere compliance with federal labeling requirements in and of itself creates a conflict preemption.

Vermont S. Ct. Oral Arg. Tr. at 7 (Oct. 5, 2007).

between FDA and Wyeth] nor any other evidence presented to the jury indicated that the FDA wished to preserve the use of IV push as a method of administering Phenergan."); 19a ("There is no evidence that the FDA intended to prohibit defendant from strengthening the Phenergan label [with an instruction precluding IV push] pursuant to § 314.70(c)."). For the same reason, the court also rejected Wyeth's contention that the FDA's 1987 direction to "retain verbiage in current label" was tantamount to rejecting a warning about the IV push method. *Id.* at 17a-18a. The notion that this cryptic statement precluded a warning about IV push was, the court said, "an unsupported hypothesis" because "the rejected [Wyeth] proposal would not have eliminated IV push as an option for administering Phenergan." *Id.* at 18a; *see id.* at 4a-5a n.1 (Wyeth's proposal).

Finally, the court dismissed Wyeth's claim for deference to the FDA's 2006 regulatory preamble, which asserts that, in limited circumstances, state failure-to-warn claims are preempted by the FDA's approval of drug labeling. *Id.* at 24a. Declining to address Ms. Levine's claim that the 2006 preamble was ineffective because it was promulgated without the requisite notice and comment, *id.* at 25a, the court held that the preamble was neither entitled to *Chevron* deference nor had the "power to persuade" under *Skidmore v. Swift & Co.*, 323 U.S. 134, 140 (1944)). *See id.* at 25a-26a. The agency's claim of conflict with federal law, the Vermont Supreme Court held, did not warrant deference because it was flatly at odds with both the FDA's regulation permitting manufacturers "to add or strengthen a warning 'to increase the safe use of the drug product' without prior FDA approval," Pet. App. 26a (quoting 21 C.F.R. § 314.70(c)(6)(iii)(C)), and with Congress's express directive that state law concerning prescription drugs be superseded only when it poses a "'direct and positive conflict' with federal law." *Id.* (quoting 76 Stat. 793).

REASONS FOR DENYING THE WRIT

A. There Is No Division In Appellate Authority On The Question Presented.

No appellate court – federal or state – has ever held that the FDA's drug approval authority or its authority over drug labeling preempts a state-law tort suit, whether premised on the manufacturer's failure to warn or on any other ground. To the contrary, every appellate court to have addressed the issue has ruled that FDA approval or compliance with FDA regulations does not preempt any state-law damage claims. *See, e.g., Tobin v. Astra Pharm. Prods., Inc.*, 993 F.2d 528, 537 (6th Cir.), *cert. denied*, 510 U.S. 914 (1993); *Osburn v. Anchor Labs.*, 825 F.2d 908, 911-13 (5th Cir. 1987), *cert. denied*, 485 U.S. 1009 (1988); *Wells v. Ortho Pharm. Corp.*, 788 F.2d 741, 746 (11th Cir.); *cert. denied*, 479 U.S. 950 (1986); *Feldman v. Lederle Labs.*, 592 A.2d 1176, 1185-97 (N.J. 1991), *cert. denied*, 505 U.S. 1219 (1992); *Kurer v. Parke, Davis & Co.*, 679 N.W.2d 867, 875 (Wis. App. 2004) ("As numerous courts have concluded, FDA regulations do not preempt the imposition of state common law liability for failure to warn claims.") (citations omitted). Thus, there is no conflict in appellate authority and, for that reason alone, no justification for this Court's intervention.[3]

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[3]In addition to the unanimity among appellate courts, the great majority of trial courts to have addressed the question have come to the same conclusion. *See, e.g., Jackson v. Pfizer, Inc.*, 432 F. Supp. 2d 964 (D. Neb. 2006); *Laisure-Radke v. Par Pharm., Inc.*, 426 F. Supp. 2d 1163, 1169 (W.D. Wash. 2006); *Peters v. Astrazeneca, LP*, 417 F. Supp. 2d 1051, 1054-57 (W.D. Wis. 2006); *Witczak v. Pfizer, Inc.*, 377 F. Supp. 2d 726, 728-32 (D. Minn. 2005); *Cartwright v. Pfizer, Inc.*, 369 F. Supp. 2d 876, 881-87 (E.D. Tex. 2005); *McNellis v. Pfizer, Inc.*, 2005 WL 3752269 (D.N.J. Dec. 29, 2005); *Zikis v. Pfizer, Inc.*, 2005 WL 1126909 (N.D. Ill. May 9, 2005);

(continued...)

B. Wyeth Seeks Review On A Question Not Presented By This Case.

The question presented by Wyeth is whether the "labeling judgments" made by the FDA regarding a drug's safety and efficacy preempt state-law product liability claims premised on "differing label judgments." Pet. i. This case does not present that question because the Vermont Supreme Court correctly found, as a matter of fact, that Ms. Levine's recovery

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[3](...continued)

Motus v. Pfizer, Inc., 127 F. Supp. 2d 1085, 1091-1100 (C.D. Cal. 2000), *aff'g dismissal on other grounds*, 358 F.3d 659 (9th Cir. 2004); *In re Paxil Litig.*, 2002WL 31375497, *1 (C.D. Cal. Oct. 18, 2002); *Eve Sandoz Pharm. Corp.*, 2002 WL 181972 (S.D. Ind. Jan. 28, 2002); *Caraker v. Sandoz Pharm. Corp.*, 172 F. Supp. 2d 1018, 1029-44 (S.D. Ill. 2001); *Globetti v. Sandoz Pharm. Corp.*, 2001 WL 419160 (N.D. Ala. Mar. 5, 2001); *Mazur v. Merck & Co.*, 742 F. Supp. 239, 245-48 (E.D. Pa. 1990); *Kociemba v. Searle & Co.*, 680 F. Supp. 1293, 1298-1300 (D. Minn. 1988); *Graham v. Wyeth Labs.*, 666 F. Supp. 1483, 1488-93 (D. Kan. 1987);*Stephens v. G.D. Searle*, 602 F. Supp. 379, 382 (E.D. Mich. 1985).

The prevailing view that the FDCA does not preempt state-law failure-to-warn claims is consistent with the entrenched common-law rule that compliance with federal statutes and regulations may be considered by the finder of fact in determining a manufacturer's liability, but is not a complete defense to a products liability claim. *Restatement of Torts (Third) – Products Liability* § 4(b) (Am. Law Inst. 1988); *see, e.g., McEwen v. Ortho Pharm. Corp.*, 528 P.2d 522, 534 (Or. 1974) (citing cases); *Stevens v. Parke, Davis & Co.*, 507 P.2d 653, 661 (Cal. 1973). The jury in this case was instructed accordingly, without objection from Wyeth. *See* Jury Instructions, Printed Case, vol. II, at 348 ("You may consider evidence of compliance by Wyeth with FDA requirements in obtaining approval for the Phenergan warning. Compliance with FDA requirements does not by itself establish that the warning was adequate for purposes of this case. You must decide whether the instructions and warnings were adequate based upon all the evidence presented in this trial including evidence about the FDA process.").

was *not* based on a labeling judgment different from a labeling judgment made by the FDA.

1. Wyeth has phrased the question presented to try to take advantage of the scant trial court authority that holds that, in narrow circumstances, certain state-law failure-to-warn claims are preempted by the FDA's specific regulatory judgments regarding a particular prescription drug label. For instance, in *Needleman v. Pfizer Inc.*, 2004 WL 1773697 (N.D. Tex. Aug. 6, 2004), the plaintiff claimed that the manufacturer of the anti-depression drug Zoloft, one of a family of drugs known as SSRIs, had failed adequately to warn of Zoloft's association with certain side-effects that led to the plaintiff's husband's suicide. The court found the plaintiff's claim preempted, but only because of the highly unusual and intensive post-marketing FDA reevaluation of SSRI labeling. As the court put it: "[T]he FDA conducted reviews of the issue in 1991, 1992, 1997, and 2002, each time finding no scientific basis for a warning that SSRIs cause suicide. The government concluded that any warning suggesting a link between SSRIs and suicide would be false, misleading, contrary to the public interest, and should not be given." *Id.* at *2. The court thus concluded that "Plaintiffs' state law failure to warn claim is preempted by the FDCA and the FDA's rulings on the warnings required for Zoloft." *Id.* at *5.

The other district court cases cited by Wyeth generally fall into the same category; they find preemption where the failure to warn upon which the plaintiff's damages claim was premised was found to be at odds with specific findings made by the FDA on the exact same topic. *See Colacicco v. Apotex, Inc.*, 432 F. Supp. 2d 514 (E.D. Pa. 2006) (finding preemption in an SSRI case); *In re Bextra & Celebrex Marketing Sales Practices and Prod. Liab. Litig.*, 2006 WL 2374742 (N.D. Cal. 2006) (finding preemption of one claim premised on an

"attempt to require Pfizer to include in its Celebrex promotion a warning which the FDA has considered and found to be scientifically unsubstantiated," but rejecting preemption of another claim where FDA had made no similar finding).[4]

In our judgment, the district court decisions on which Wyeth relies are incorrect because, among other reasons, they fail to give sufficient weight to Congress's narrow understanding of preemption under the FDCA and the governing FDA regulations under which manufacturers may amend drug labels to strengthen warnings, contraindications, and instructions to protect patient health and safety. For present purposes, however, these cases are important because of their narrow scope, and the distinction that they draw between situations in which the FDA has made a specific determination contrary to the state-law warning that underlies the plaintiff's claim, on the one hand, and run-of-the-mill failure-to-warn cases such as Ms. Levine's, on the other. *See In re Bextra*, 2006 WL 2374742, at *10 (contrasting a case involving "a warning which the FDA has considered and found to be

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[4]The other district court case cited by Wyeth, *Ehlis v. Shire Richwood, Inc.*, 233 F. Supp. 2d 1189 (D.N.D. 2002), found preemption of a state-law claim in an alternative holding that contained no analysis of the degree of FDA involvement over the drug label in question and relied almost exclusively on precedent regarding the *express preemption* provision of the federal medical device law. *See id.* at 1197-98. Wyeth (at 17) suggests that *Ehlis* was affirmed on preemption grounds, but, in fact, it was affirmed solely on state-law grounds wholly unrelated to preemption. *See Ehlis v. Shire Richwood, Inc.*, 367 F.3d 1013 (8th Cir. 2004). Like *Ehlis*, *Horn v. Thoratec Corp.*, 376 F.3d 163 (3d Cir. 2004), cited in the petition at 21 and 29, is inapposite because it construed the medical device law's express preemption provision. *See* Pet. App. 14a ("In Horn, the Third Circuit relied on an express preemption clause in the FDCA that relates only to medical devices. . . . Because no such clause exists for prescription drugs, Horn's reasoning does not apply to this case.").

scientifically unsubstantiated" with "a case where the FDA has not considered the risks of which plaintiffs claim the drug manufacturer should have warned[.]") The Vermont Supreme Court drew the very same distinction, contrasting Ms. Levine's case with *Needleman*, where the finding of preemption was based "on the facts of the *Zoloft* litigation" and the FDA's specific rejection of "the warning advocated by the plaintiff." Pet. App. 13a.

This case is at the other end of the spectrum from a case like *Needleman*. As discussed above (at 9-10, 12), no record evidence suggests that the FDA even considered the particular safety ramifications of the IV push method for Phenergan administration, let alone specifically rejected a warning that would have precluded or limited its use. *See, e.g., id.* at 17a (finding no support for Wyeth's speculation that the FDA believed "it would have harmed patients [to] eliminat[e] IV push as an option for administering Phenergan"), 19a (finding "no evidence" that FDA wanted to preserve IV push or to preclude a warning against it). As the Vermont Supreme Court explained, Wyeth "has provided a number of letters exchanged by the FDA and defendant regarding Phenergan's label, but these letters do not indicate the FDA's opinion of the value of IV-push administration." *Id.* at 17a. Thus, as this case comes to this Court, it does not implicate the question presented or the small minority of district court rulings that find preemption of state-law duty-to-warn claims based on specific FDA labeling judgments concerning particular prescription drug labels.[5]

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[5]The letters referred to by the Vermont Supreme Court are included in the appendix to the Petition. They do not mention, let alone discuss, the safety or efficacy of the IV push method. Wyeth's suggestion (at 6-9) that the FDA affirmatively sanctioned use of the IV push method is simply wrong. The label warnings cited by Wyeth concern the undisputed risks of

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2. For much the same reasons, the petition also does not present any genuine issue regarding the applicability of the 2006 FDA regulatory preamble on which Wyeth relies. The petition fails to describe the preamble's operative legal standard under which, in the FDA's view, the agency's labeling approval will preempt a state-law claim premised on a failure to warn. That legal standard – which includes two bases for preemption – warrants a full quotation:

> FDA believes that State laws conflict with and stand as an obstacle to achievement of the full objectives and purposes of Federal law when they purport to compel a firm to include in labeling or advertising a statement that FDA has considered and found scientifically unsubstantiated. In such cases, including the statement in labeling or advertising would render the drug misbranded under the act (21 U.S.C. 352(a) and (f)). The agency believes that State law conflicts with and stands as an obstacle to achievement of the full objectives and purposes of Federal law if it purports to preclude a firm from including in labeling or advertising a statement that is included in prescription drug labeling. By complying with the State law in such a case and removing the statement from labeling, the firm would be omitting a statement required under § 201.100(c)(1) as a condition on the exemption from the

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[5](...continued)
arterial exposure to Phenergan and the IV drip method of administration, that is, administration through a hanging IV bag, not the IV push method. The petition's statement that "[b]etween 1967 and 1981, FDA worked closely with Wyeth through a series of communications and at least one in-person meeting to refine Phenergan's warnings with respect to IV push administration[,]" Pet. 6-7, has no basis in the record and, not surprisingly, is not accompanied by *any* citation.

> requirement of adequate directions for use, and the omission would misbrand the drug under 21 U.S.C. 352(f)(1). The drug might also be misbranded on the ground that the omission is material within the meaning of 21 U.S.C. 321(n) and makes the labeling or advertising misleading under 21 U.S.C. 352(a) or (n).

71 Fed. Reg. at 3935, Pet. App. 136a.[6]

After setting out the foregoing legal standard, the preamble provides six examples of state-law claims that the FDA believes would give rise to preemption, only two of which even arguably bear on Wyeth's claim for preemption here: "claims that a drug sponsor breached an obligation to warn by failing to include a statement in labeling or advertising, the substance of which had been proposed to FDA for inclusion in labeling, if that statement was not required by FDA at the time

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[6]Wyeth erroneously claims support for its expansive view of the preamble in recent FDA amicus briefs but ignores their key passages. For instance, the agency's amicus brief in *Perry v. Novartis Pharmaceuticals*, Civ. No. 05-5350 (E.D. Pa.) (filed Sept. 22, 2006) (hereafter "*Perry* Br."), cited in the petition at 28, references as the operative legal principle the exact portion of the preamble quoted above. *Perry* Br. 10. The FDA brief also explains:

> A failure-to-warn claim is not preempted merely because it imposes liability for a manufacturer's failure to provide a warning that has not yet been required by FDA. Federal regulations explicitly recognize that manufacturers can, and in some limited instances must, modify their labels to add new warnings of hazards associated with the drug without awaiting prior FDA approval. *See* 21 C.F.R. § 314.70(c)(7); 21 C.F.R. § 201.56. [Although the FDA may ultimately reject such a labeling change,] "[t]o the extent, therefore, that the defendants argue that federal preemption bars *any* failure-to-warn claim premised on a drug manufacturer's failure to provide a warning not contained in the drug's approved labeling, the defendants are incorrect."

Id. at 10-11.

plaintiff claims the sponsor had an obligation to warn"; and "claims that a drug sponsor breached an obligation to warn by failing to include in labeling or in advertising a statement the substance of which FDA has prohibited in labeling or advertising[.]" *Id.* at 3936, Pet. App. 138a-139a.

The foregoing discussion of the factual record, and the Vermont's Supreme Court's findings based on it, demonstrate that Ms. Levine's claims did not "purport to compel [Wyeth] to include in "labeling or advertising a statement that FDA ha[d] considered and found scientifically unsubstantiated." Nor did they "purport[] to preclude [Wyeth] from including in labeling or advertising a statement that is included in prescription drug labeling." As explained above, there is no evidence that the FDA considered a statement that would have precluded the use of IV push, let alone found it scientifically unsubstantiated, and no one has suggested that Ms. Levine sought to preclude a statement that was on the approved label. Her claim is that Wyeth should have included an instruction that would have foreclosed use of the IV push method for administering Phenergan.

The irrelevance of the 2006 preamble to this case thus underscores the conclusion that, *as it comes to this Court,* this case does not genuinely implicate the question presented, and it would not do so unless this Court were first to overturn the Vermont courts' factual findings. The petition tacitly understands this problem and thus spills considerable ink attempting to show that the FDA considered and rejected an instruction precluding the IV push method and made a conscious, affirmative decision to retain that method for administering Phenergan. Pet. 6-9. The difficulty with making that argument below, as the Vermont Supreme Court found, was that it has no basis in the factual record. That difficulty is compounded at this juncture because, except in extraordinary

circumstances, this Court does not grant review "when the asserted error consists of erroneous factual findings." S. Ct. Rule 10. For this reason as well, review should be denied.

C. This Case Is An Inappropriate Vehicle For Deciding Whether The FDA's 2006 Regulatory Preamble Is Entitled To Deference Because The Preamble Post-Dates The FDA's Purportedly Preemptive Labeling Decisions Regarding Phenergan.

The petition argues that the courts must defer to the FDA's views on preemption as set forth in the agency's 2006 preamble. Pet. 27-30. As explained in the previous section, Ms. Levine's recovery would not be preempted under the express terms of the preamble. Moreover, the FDA's views on preemption of state-law damages claims have never been the subject of *any* appellate decision. Indeed, only one appellate court has even mentioned those views, and, in that case, the Second Circuit suggested in dicta that deference would be unwarranted because "an agency cannot supply, on Congress's behalf, the clear legislative statement of intent required to overcome the presumption against preemption." *Desiano v. Warner-Lambert & Co.*, 467 F.3d 85, 97 n.9 (2d Cir. 2006) (quoting *Alexander v. Sandoval*, 532 U.S. 275, 291 (2001) ("Agencies may play the sorcerer's apprentice but not the sorcerer himself.")).

Even if the Court were inclined, absent any appellate authority on the topic, to consider whether the 2006 preamble is entitled to deference, this case is not an appropriate vehicle for doing so because deference may not be accorded retroactively, that is, in a situation where the FDA labeling decisions said to have preemptive effect pre-date the FDA's views for which deference is claimed. An agency's legislative rule promulgated pursuant to a proper congressional grant of authority, like a congressional statute, will not have retroactive

effect unless the rule's text demands it and the congressional delegation includes the authority to issue retroactive rules. *Bowen v. Georgetown Univ. Hosp.*, 488 U.S. 204, 208-09 (1988). That is so because regulations that are properly authorized by Congress, like congressional statutes themselves, have the effect of law. The same principle applies in a situation where, as Wyeth asserts here, the agency's views expressed in a format other than an agency regulation are claimed to have the force of law. *See* Pet. 29-30.

In our view, Congress has not delegated to the FDA the authority to patrol the borderline between federal regulatory power and state tort law, and, even if it had, deference to the 2006 preamble would be unwarranted for a host of reasons. *See infra* at 26-29. But assuming that this Court were inclined to consider whether the 2006 preamble is entitled to deference, it should do so only in a case where, at the relevant time, the federal legal command said to have preemptive effect – the 2006 preamble – arguably could have been in conflict with the state law said to be preempted.

But that is impossible here. According to Wyeth, the most recent relevant labeling decision regarding Phenergan was made in September 1998. *See* Pet. 8 (referring to FDA letter reproduced at Pet. App. 164a). In *1998*, federal law regarding the preemptive effect of FDA approval of drug labeling could not have included the *2006* preamble. One commentator has made this point in the context of the SSRI litigation, in which, as in Ms. Levine's case, the agency's decisions regarding the product label pre-dated the agency's view that certain tort claims are preempted: "The FDA henceforth might characterize as misbranding any [future] labeling change that the FDA itself declines to require. . . . [W]hat the FDA cannot do – with or without *Chevron* deference – is to impose that characterization upon past events where the legal landscape offered only a

glimmer, at best, of such a view. The prerogative of filling gaps and resolving ambiguities in statutes does not embrace the rewriting of history." Richard Nagareda, *FDA Preemption: When Tort Law Meets The Administrative State*, 1 J. Tort Law iss.1, art. 4, at 35 (2006), available at www.bepress.com/jtl/vol1/iss1/art4/; *see also* Pet. App. 26a (noting retroactivity problem).[7]

In sum, if and when this Court wishes to consider whether and in what circumstances the FDA's drug labeling authority preempts state-law failure-to-warn claims, including the legal effect, if any, of the FDA's views on those questions, it should do so in a case, unlike this one, where the relevant FDA labeling judgments post-date the agency statements for which deference is claimed.[8]

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[7]The agency is entitled to its opinion on the preemptive effect of the FDCA on state-law tort claims – that is, without treating the 2006 preamble as part of the body of substantive federal law – but it is entitled to no deference on that "pure question of statutory construction," *INS v. Cardoza-Fonseca*, 480 U.S. 421, 446 (1987), or, at best, only to the weight attributable to the preamble's persuasive force. *See Skidmore v. Swift & Co.*, 323 U.S. 134, 140 (1944). Wyeth, however, seeks substantial deference to the 2006 preamble of the kind that flows from an agency's proper exercise of its delegated law-making authority. *See* Pet. 29 (claiming "FDA's substantive interpretation of its own regulations should be entitled to considerable deference"); *see also In re Bextra*, 2006 WL 2374742, at *6-*7 (according *Chevron*-type deference to 2006 preamble). That purported addition to federal law can only be applied prospectively.

[8]This case is a poor vehicle for considering the question presented for the related reason that the Phenergan labeling was originally approved in 1955 before any efficacy review and thus without any risk-benefit analysis. Although the label went through some subsequent FDA review and revision, the situation presented by this case raises the question whether the drug's serious risks were searchingly weighed against its benefits when used

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D. Wyeth Is Wrong On The Merits.

As discussed above, there is no basis for the Court to look past its ordinary, time-honored restraints on review. Moreover, the Vermont Supreme Court resolved the merits correctly.

1. The parties agree that the FDCA does not expressly preempt state-law damages claims or occupy the field of prescription drug regulation. Thus, the question here is whether Ms. Levine's state-law claim is impliedly preempted because it actually conflicts with federal law, that is, whether her recovery renders Wyeth's compliance with state and federal law physically impossible or whether Wyeth's compliance with state law would erect an impermissible obstacle to the accomplishment of federal objectives.[9]

As the Vermont Supreme Court held, it would not have been impossible to comply with a state-law duty to warn against IV push and federal labeling requirements because those requirements expressly give manufacturers the right to revise labels to include contraindications, warnings, and instructions that enhance patient safety without prior FDA approval. 21 C.F.R. § 314.70(c)(6)(iii)(A), (C). And FDA regulations say that "labeling *shall* be revised to include a warning as soon as

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[8](...continued)
to combat a non-life threatening common malady such as nausea. *See* Tr. vol. I, at 236, 249-50 (discussing ramifications of fact that FDA did not conduct risk-benefit analysis at time Phenergan was approved).

[9]Wyeth's attempt to turn the Vermont Supreme Court's brief mention of the presumption against preemption into a basis for review is meritless. The presumption is based on a long, unbroken line of authority from this Court, including many cases involving claims that federal regulatory schemes preempt state tort law. It applies with full force here. *See* Pet. App. 7a (citing cases).

there is reasonable evidence of an association of a serious hazard with a drug." 21 C.F.R. § 201.80(e) (emphasis added). Based on these regulations, the FDA itself has stated that a "failure-to-warn claim is not preempted merely because it imposes liability for a manufacturer's failure to provide a warning that has not yet been required by FDA." *Perry* Br. 11.

Moreover, it is not physically impossible for Wyeth to comply with federal requirements and the state court's damages verdict, which does not require Wyeth to alter its conduct but only to pay damages to Ms. Levine. As the Court recently explained in *Bates v. Dow Agrosciences LLC*, a "requirement is a rule of law that must be obeyed; an event, such as a jury verdict, that merely motivates an optional decision [to re-label the product] is not a requirement." 544 U.S. 431, 443 (2005).[10]

Ms. Levine's recovery likewise poses no obstacle to the accomplishment of federal objectives. Wyeth claims that the Vermont Supreme Court's decision regarding obstacle preemption is at odds with this Court's view that federal "savings clauses" do not bar the application of ordinary conflict preemption principles. Pet. 23. The Vermont court did not eschew those principles. Rather, it correctly held that, because the FDCA limits preemption to "direct and positive conflict[s]" between state and federal law, Pub. L. 87-781, § 202, there can be no obstacle to federal objectives where a manufacturer is able to comply with applicable state and federal duties. *See* Pet. App. 21a-23a. In any event, as explained above, the FDA never considered and found scientifically unsubstantiated a warning foreclosing or limiting the IV push method for administering Phenergan. Given the dangers of the IV push method, the verdict in Ms. Levine's favor advanced, not undermined,

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[10]*See also, e.g., Sprietsma v. Mercury Marine*, 537 U.S. 51, 64 (2002); *Goodyear Atomic Corp. v. Miller*, 486 U.S. 174, 185-86 (1988).

federal health and safety objectives. *See Bates*, 544 U.S. at 450-51. Moreover, because FDA regulations expressly allow Wyeth to warn against use of the IV push method, Ms. Levine's recovery – premised on a failure to provide that warning – cannot be an obstacle to the accomplishment of such objectives. *See* Pet. App. 9a-19a. Thus, Ms. Levine's claim – whether viewed under the "impossibility" or "obstacle" prong of conflict preemption – is not preempted, and the question whether the Vermont Supreme Court mis-spoke on the nuances of implied preemption doctrine is an academic issue unworthy of review.[11]

2. Even assuming that the FDA's 2006 preamble is entitled to retroactive effect, *see supra* at 21-23, and that it applies to the facts here, *see supra* at 18-21, it should not be accorded deference for several independent reasons. Thus, the preamble provides no basis for finding preemption.

First, administrative agencies, because they are creatures of the executive branch, do not have the power to regulate with the force of law unless Congress has delegated that power to them. *See Gonzales v. Oregon*, 126 S. Ct. 904, 915-16 (2006). As noted above (at 7), Congress declined to provide a federal damages remedy in the FDCA precisely because state-law

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[11]Wyeth's reliance on *Geier v. American Honda Motor Co., Inc.*, 529 U.S. 861 (2000), is misplaced. There, the Court found that a damages suit premised on an automaker's failure to install airbags was an obstacle to the accomplishment of federal regulatory objectives because the agency had considered requiring airbags alone, but ultimately decided that automakers should have the flexibility to choose from a variety of passive restraints. *Id.* at 875-82. The more apt authority is the Court's post-Geier decision in *Sprietsma v. Mercury Marine*. There, a damages action premised on a boat manufacturer's failure to install a propeller guard was not preempted where the federal agency considered whether to require such guards but ultimately took no action on the topic. 537 U.S. at 60-62, 65-67. *Sprietsma* applies here in spades because the FDA did not consider, let alone reject, a warning precluding the use of IV push.

damages remedies were available. Therefore, Congress hardly can be said to have authorized the FDA to supersede damages remedies traditionally provided by the states. *See also Adams Fruit v. Barrett*, 494 U.S. 638, 650 (1990) (declining to defer to agency's view regarding preemptive reach of federal statute's right of action, and noting that, despite agency's authority to issue relevant safety standards, "an agency may not bootstrap itself into an area in which it has no jurisdiction.") (quoting *Federal Maritime Comm'n v. Seatrain Lines, Inc.*, 411 U.S. 726, 745 (1973)).

Second, the preamble lacks the requisite formality to be accorded deference. *See United States v. Mead Corp.*, 533 U.S. 218, 228 (2001). The preamble is not part of the FDA's new labeling regulation and does not appear in the Code of Federal Regulations. *See id.* at 229-30. Indeed, FDA regulations treat a regulatory preamble as an "advisory opinion," 21 C.F.R. § 10.85(d)(1), which cannot bind the public in an administrative or court proceeding because it is not "a legal requirement." *Id.* § 10.85(j).

Third, even assuming that a regulatory preamble could in some circumstances add to the preemptive force of federal law, the 2006 preamble cannot do so because its views on preemption were not subject to the notice-and-comment process required to give them such force under the Administrative Procedure Act, 5 U.S.C. § 553. As explained above, when the FDA proposed the new labeling regulations, it stated that they would not preempt state law. 65 Fed. Reg. at 81103 ("FDA has determined that this proposed rule does not contain policies that have federalism implications or that preempt State law."). Although the agency asked whether the "Highlights" section of the proposed labeling rule should be revised to address liability concerns, *id.* at 81086, the agency never intimated that it was contemplating a position that embraced preemption of any state-

law tort claims, whether or not related to the "Highlights" section, and thus it did not provide the notice demanded by section 553. *See, e.g., Envtl. Energy Project v. EPA*, 425 F.3d 992, 996 (D.C. Cir. 2005) (citing cases) (final rule must be "logical outgrowth" of proposed rule, which must provide reasonable basis to anticipate change and not require public to "divine [agency's] unspoken thoughts") (citation omitted).

Fourth, deference is often inappropriate where an agency's position lacks consistency. *See Mead*, 553 U.S. at 228. Here, as noted above (at 7-8), the FDA originally took a no-preemption position in the very rulemaking that resulted in the 2006 preamble, and, until recently, it has consistently maintained that federal drug regulation does not affect state-law damages liability. The Court repeatedly has refused to give weight to agency flip-flops regarding tort preemption. *See Bates*, 544 U.S. at 449 ("The notion that FIFRA contains a nonambiguous command to pre-empt the types of tort claims that parallel FIFRA's misbranding requirements is particularly dubious given that just five years ago the United States advocated the interpretation that we adopt today."); *Norfolk Southern Ry. Co. v. Shanklin*, 529 U.S. 344, 356 (2000). The government's position need not be immutable, but it cannot change willy-nilly, as it has here, without the agency providing concrete examples showing that tort recoveries have undermined federal drug regulation.

Finally, deference is inappropriate because the FDA's views are unpersuasive. *See Mead*, 553 U.S. at 228. As noted, the FDCA permits preemption of state law only when the two are in "direct" conflict. Assuming that a state-law failure-to-warn damages verdict may ever constitute such a direct conflict, it cannot do so when the agency's own regulations require manufacturers to revise their labels to protect the public health and permit such changes without prior agency approval.

CONCLUSION

The petition for a writ of certiorari should be denied.

Respectfully submitted,

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